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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,937	10/17/2001	Karin Drechsel	1/1156	6299

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BOEHRINGER INGELHEIM CORPORATION
900 RIDGEBURY ROAD
P. O. BOX 368
RIDGEFIELD, CT 06877

EXAMINER
HAGHIGHATIAN, MINA

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 07/17/2003

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/981,937	DRECHSEL ET AL.	
	Examiner	Art Unit	
	Mina Haghighatian	1616	

-- The MAILING DATE of this c mmunication appears on the c ver sheet with the correspondence address --

Peri d for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *05 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disp sition of Claims

4)☒ Claim(s) *1-95* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-95* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendments filed 05/05/03 are entered. No new claims are added and no claim is cancelled. Claims 1-95 are pending.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-37, 50, 53-80 and 93 are rejected under 35 U.S.C. 102(e) as being anticipated by Freund et al (US 2001/0008632).

Freund teach pharmaceutical preparations in the form of aqueous solutions for the production of propellant-free aerosols for inhalation for the therapy of obstructive lung diseases. Pharmaceuticals intended for inhalation are dissolved in an aqueous or ethanolic solution or a solvent mixture of ethanol and water. The amount of dissolved pharmaceutical in the preparation is between 0.001 and 30%, and preferably between 0.05 and 3%. All substances which are suitable for application by inhalation and which are soluble in the specified solvent can be used as pharmaceuticals in the new

preparation. Of especial interest are betamimetics, anticholinergics, antiallergic, antihistamines and steroids, as well as combinations of these active ingredients (sections [0001] to [0007]).

Freund teaches that addition of an effective amount of a complexing agent, such as, EDTA, citric acid, ascorbic acid and their salts, and more especially disodium salt of ethylenediaminetetraacetic acid, eradicates the problem of spray anomalies. The effective quantity of complexing agent Na-EDTA is between 10 and 100 mg/100 ml. Also if necessary, ethanol can be added to increase solubility up to 70% by volume. Other adjuvants such as preservatives, especially benzalkonium chloride can be added in amounts of between 8 and 12 mg/100 ml (sections [0009] to [0013]).

Freund discloses a list of compounds which can be used as active ingredients, singly or in combination, in the aqueous pharmaceutical preparation. In individual cases, it may be required to add a higher quantity of ethanol or a solution mediator to improve solubility. The list includes; tiotropium bromide, budesonide, beclomethasone, disodium cromoglycate, etc. The solutions are set to a pH of 3.2 to 3.4 with 0.1 or 1 N HCL in 100 ml of finished preparation (see sections [0014] to [0046] and [0055]).

Claims 1-37, 50, 53-80 and 93 are rejected under 35 U.S.C. 102(e) as being anticipated by Bozung et al (6,433,027).

Bozung et al teach medicament compositions based on anticholinergic compounds which have a long-lasting effect and betamimetics, which have a long-

lasting effect, processes for their production and their use in the therapy of respiratory ailments, especially COPD (col. 1, lines 11-16). Tiotropium bromide monohydrate is the preferred anticholinergic (col. 5, lines 51-55). The medicaments for inhalation are dissolved in an aqueous or ethanolic solution, wherein solvent mixtures of ethanol and water are also suitable. Other adjuvants, such as preservatives, e.g. benzalkonium chloride in concentration range of 8 to 12 mg/100 ml are added. Complex formers like EDTA, citric acid, ascorbic acid can be added. The medicament is present in an amount of 0.001 to 5% (see col. 6, line 39 to col. 7, line 40).

Claims 38-49, 51, 52, 81-92, 94 and 95 are rejected under 35 U.S.C. 103(a) as being unpatentable over Freund et al as applied to claims 1-37, 50, 53-80 and 93 above, and further in view of Weston et al (WO 9114468).

Freund et al, discussed above, lacks specific teachings on the inhalation device.

Weston et al discloses a metered dose inhaler which incorporates metering means for metering a quantity of fluid, and the atomizing means is provided by a mechanical break up device through which the metered quantity of fluid is passed to atomise it when it is subject to said increase in pressure (page 7, lines 5-9). For dispensing a spray of an aqueous solution of a medicament for inhalation into lungs, the droplet size is desirably less than 10 micrometers, typically 2 to 6 micrometers.

Weston also discloses that very high pressures can be generated in the pump cylinder or pressure and nozzle orifice diameters can be used, for example up to 100 micrometers, typically greater than 30 to 50 micrometers. The preferred pressures are

from 50 to 400 bar, and more preferably from 100 to 350 bar with nozzle orifice of from 1 to 12 micrometers (page 12, lines 1-32).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to have utilized the preparation of Freund et al by incorporating it in a device suitable for such preparations and because it is made simpler in design and cheaper to produce and suited to its function, as taught by Weston et al.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure, Jaeger et al (5,964,416).

Jaeger et al teaches a device adapted for use in an atomizer to produce an inhalable aerosol of a liquid medicament without the use of propellant gas. The atomizer is preferably a metered dose inhaler the hollow piston with valve member exerts a pressure of about 50 to 600 bar on the fluid at its high pressure end at the moment of release of the spring. The nozzle is microstructured and consists of two plates of glass and/or silicone firmly joined together, of which at least one plate has one or more microstructured channels which connect the nozzle inlet end to the nozzle outlet. At the nozzle outlet end is at least one circular or non-circular opening less than or equal to 10 micron in size. In a nozzle member having at least two nozzle openings at the outlet end, the directions of spray may be inclined relative to one another at an angle from 20 to 160 degrees (col. 5, lines 25-53).

Response to Arguments

Applicant's arguments filed 05/05/03 have been fully considered but they are not persuasive.

Applicant argues that while Freund mentions elements of applicant's invention, it does not provide any disclosure or embodiment of the combination of the applicant's claimed invention. Contrary to applicant's assertion, it was shown that Freund teaches **aqueous** medicament formulations containing all the elements of the instant claims, therefore meeting the claims. It is noted that the instant claims are drawn to compositions **comprising** (open-ended language) tiotropium, a solvent and preservative, where the solvent is **water** or water/ethanol mixture.

Applicant traversing the combination of Freund et al and Weston et al, states that Freund is deficient in teaching the formulation, therefore using device of Weston is not obvious. However, as shown above, Freund is clearly disclosing the formulation, thus it would be obvious to one of ordinary skill in the art to have implemented the nebulizer of Weston for administering the aerosolized formulation of Freund to the respiratory tract.

Applicant stated that Bozung et al is not a proper reference under 35 USC 102(b) because it was not published more than one year prior to the instant application's effective filing date. Although applicant is correct, this was due to a typographical error and Bozung et al is clearly a proper reference under 35 USC 102(e).The rejections are maintained.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mina Haghighatian whose telephone number is 703-308-6330. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0198.

Mina Haghighatian
July 2, 2003

MICHAEL G. HARTLEY
PRIMARY EXAMINER